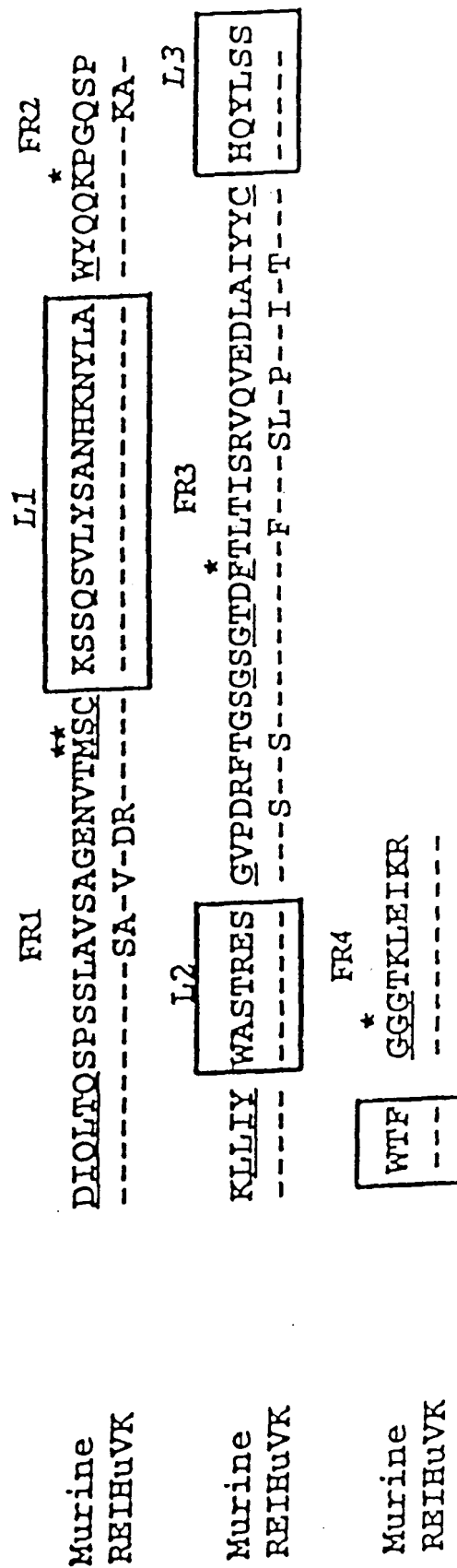


FIG. 1A



Title: IMMUNOCONJUGATES AND
HUMANIZED ANTIBODIES SPECIFIC
FOR B-CELL LYMPHOMA AND
LEUKEMIA CELLS

Inventor(s): Shui-on LEUNG et al.

Appl. No.: 09/741,843

FIG. 1B

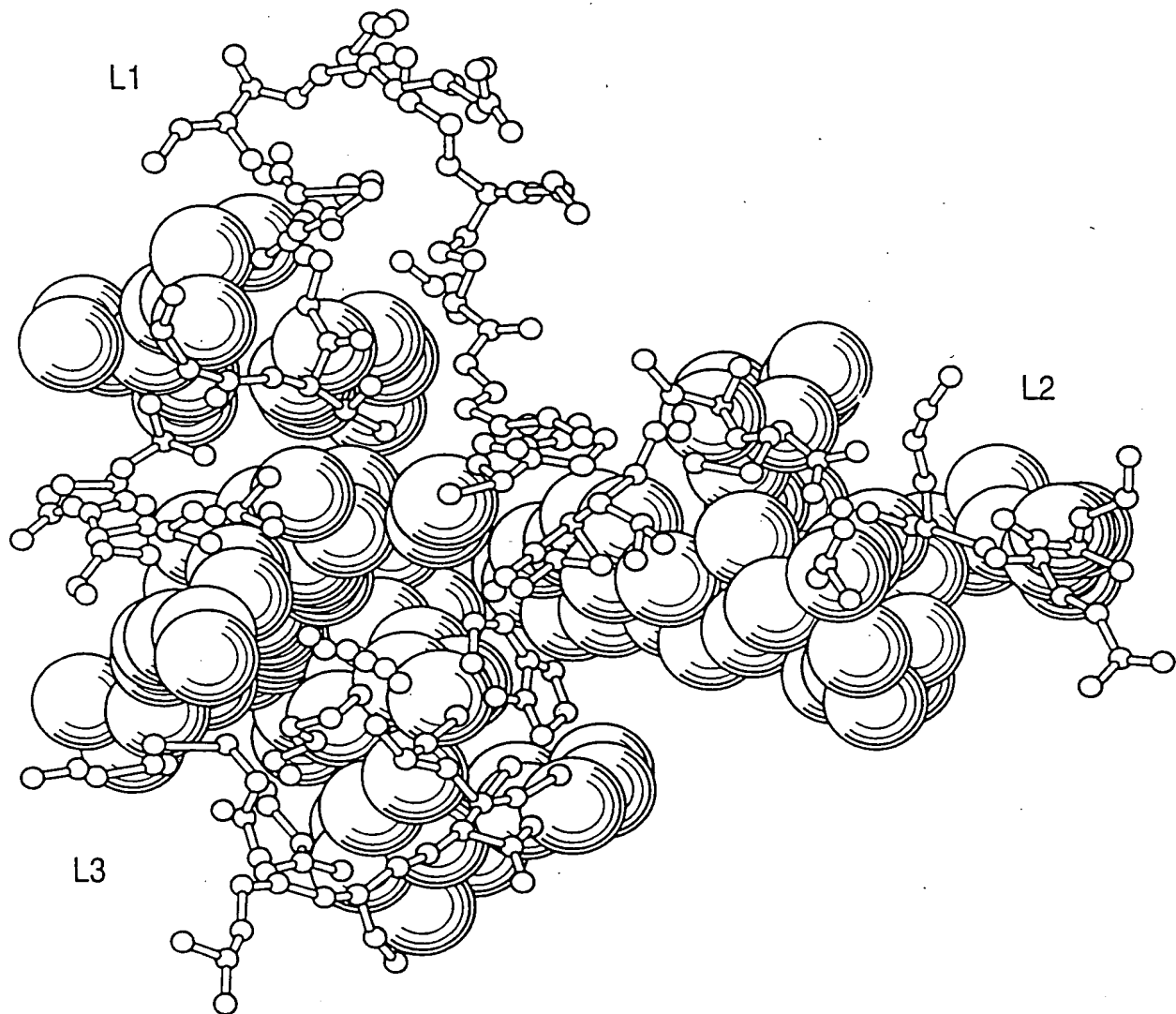
Murine EUHuVH1 EUHuVH2	FR1 QVQLQESGAELSKPGASVKMSCKASGYTFT -----Q-----VK-----S-----V----- -----VQ-----VK-----S-----V-----	H1 SYWLH ----- ----- -----	FR2 WIKQRPQGGLWIG -----VR-A----- -----VR-A-----	*
Murine EUHuVH1 EUHuVH2	H2 YINPRNDYTEYNQNFKD ----- -----	** KATLTADKSSSTAYMQLSSLTSEDSAVYYCAR -----I-----E-TN-----E-----R-----T-F-F----- -----I-----E-TN-----E-----R-----T-F-F-----	FR3 -----	*
Murine NEWMHuVH1 NEWMHuVH2	H3 RDITTFY ----- -----	FR4 WGQGTTLTVSS -----V----- -----V-----		

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LEUKEMIA CELLS

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Appl. No.: 09/741,843

FIG. 2A



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FOR B-CELL LYMPHOMA AND
LEUKEMIA CELLS

Inventor(s): Shui-on LEUNG et al.

Appl. No.: 09/741,843

FIG. 2B

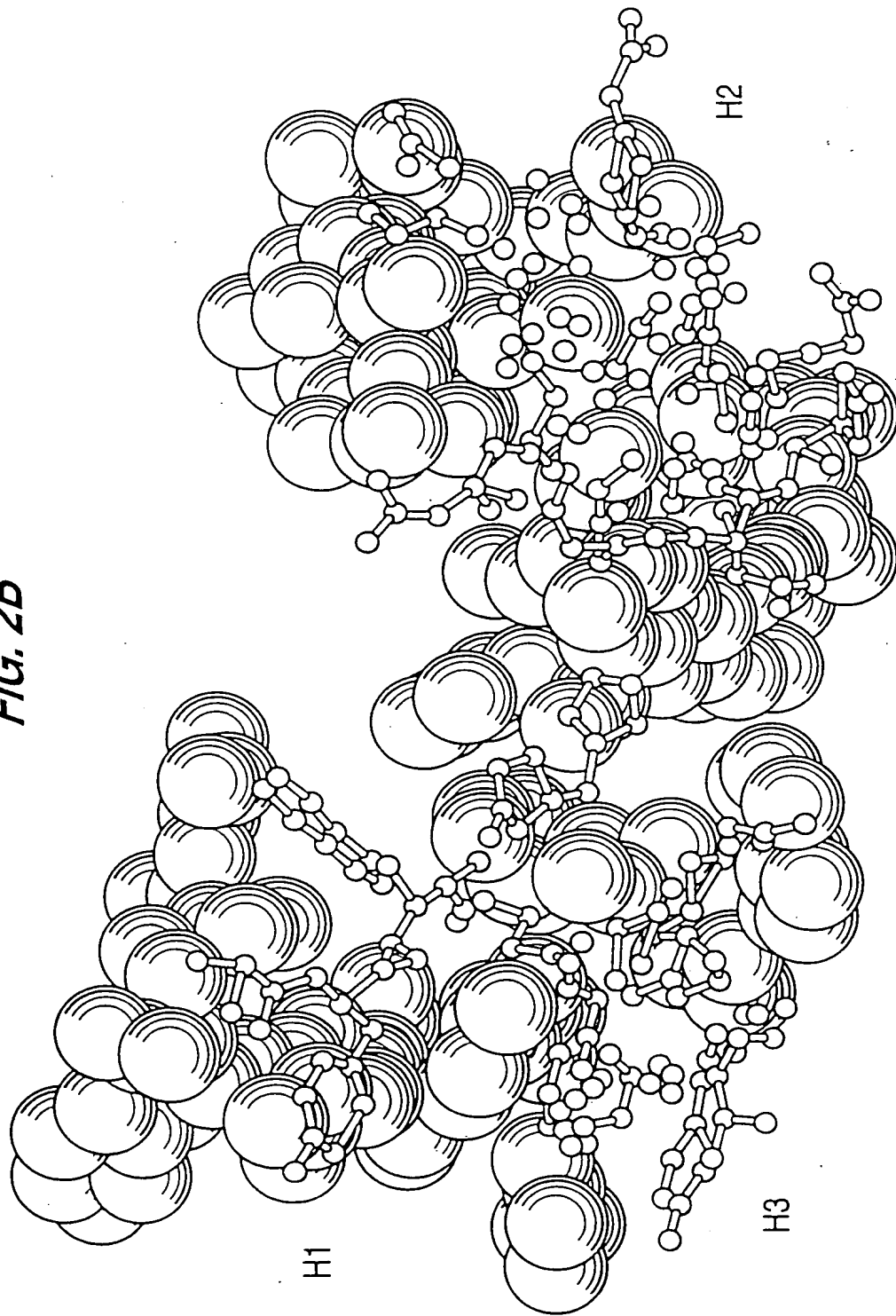


FIG. 2B

FIG. 3A

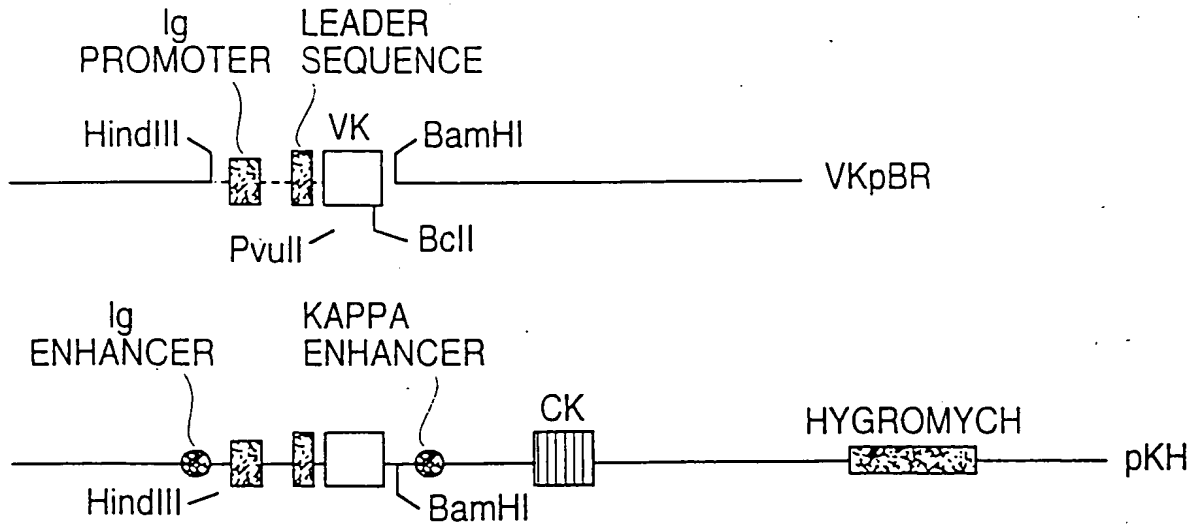
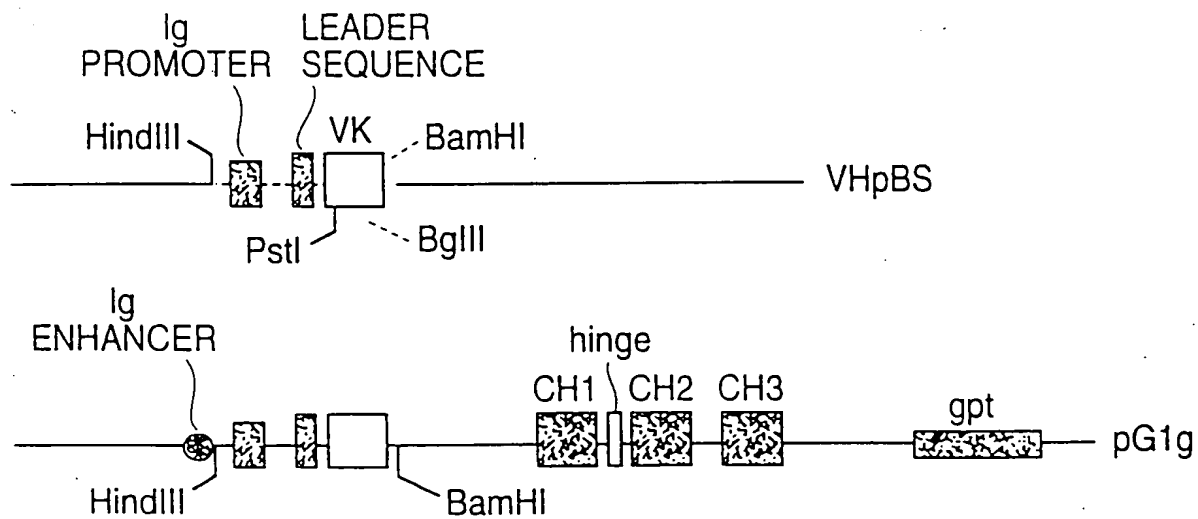


FIG. 3B



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FIG. 4A

FIG. 4A

GACATTCAGCTGACCCAGTCTCCATCATCTCTGGCTGTGTCTGCAGGAGAAAACGTCCTACT
1-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 60
CTGTAAGTCGACTGGGTCAGAGGCTAGAGAGACCGACACAGACGCTCCTCTTTTGGCAGTGA
D I Q L T Q S P S L A V S A G E N V T
ATGAGCTGTAAGTCCAGTCAAAGTGTTTATACAGTGCAAAATCACAGAAGTACTTGGCC
61-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 120
TACTCGACATTCAGGTCAGTTTCACAAAATATGTCACGTTTAGTGTTCTTGATGAACCGG
CDR1
M S C K S S Q S V L Y S A N H K N Y L A
TGGTACCAGCAGAAACAGGGCAGTCTCCTAAACTGCTGATCTACTGGGCATCCACTAGG
121-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 180
ACCATGGTCGCTTTGGTCCCGTCAGAGGATTTGACGACTAGATGACCCGTAGGTGATCC
CDR2
W Y Q Q K P G Q S P K L L I Y W A S T R
GAATCTGTGTCCTGATCGCTTCACAGGCAGCGGATCTGGACAGATTTACTCTTACC
181-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 240
CTTAGACCACAGGGACTAGCGAAGTGTCGCGCCTAGACCCCTGTCTAAAATGAGAATGG
E S G V P D R F T G S G S G T D F T L T
ATCAGCAGAGTACAAGTTGAAGACCTGGCAATTATTATTGTCACCAATACCTCTCCTCG
241-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 300
TAGTCGTCTCATGTTCAACTTCTGGACCGTTAAATAATAACAGTGGTTATGGAGAGGAGC
CDR3
I S R V Q V E D L A I Y Y C H Q Y L S S
TGGACGTTTCGGTGGAGGGACCAAGCTGGAGATCAAAACGT
301-----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 339
ACCTGCAAGCCACCTCCCTGGTTCGACCTCTAGTTTGA
W T F G G G T K L E I K R

CAGGTCCAGCTGCAGGAGTCAGGGGCTGAACCTGTCAAAAACCTGGGGCCTCAGTGAAGATG
 1 +-----+-----+-----+-----+-----+-----+-----+-----+ 60
 GTCCAGGTCGACGTCCTCAGTCCCAGACTTGACAGTTTGGACCCCGGAGTCACTTCTAC
 Q V Q L Q E S G A E L S K P G A S V K M -
 TCCTGCAAGGCTTCTGGCTACACCTTTACTAGCTACTGGCTGCACCTGGATAAAACAGAGG
 61 +-----+-----+-----+-----+-----+-----+-----+-----+ 120
 AGGACGTTCGGAAGACCGATGTGGAATGATCGATGACCGACGTGACCTATTTTGTCTCC
 S C K A S G Y T F T S Y W L H W I K Q R -
 CCTGGACAGGCTCTGGAATGGATTGGATAACATTAATCCTAGGAATGATTATACTGAGTAC
 121 +-----+-----+-----+-----+-----+-----+-----+-----+ 180
 GGACCTGTCCCAGACCTTACCTAACCTATGTAATTAGGATCCTTACTAATATGACTCATG
 CDR2
 P G Q G L E W I G Y I N P R N D Y T E Y -
 AATCAGAACTTCAAGGACAAGGCCACATTGACTGCAGACAAAATCCTCCAGCACAGCCTAC
 181 +-----+-----+-----+-----+-----+-----+-----+-----+ 240
 TTAGTCTTGAAGTTCCTGTTCGGGTGTAACCTGACGTCTGTTTAGGAGGTCGTGTCGGATG
N Q N F K D K A T L T A D K S S S T A Y -
 ATGCAACTGAGCAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGAAGGAT
 241 +-----+-----+-----+-----+-----+-----+-----+-----+ 300
 TACGTTGACTCGTCCGACTGTAGACTCCTGAGACGTCAGATAATGACACGTTCTTCCCTA
 M Q L S S L T S E D S A V Y Y C A R R D -
 ATTACTACGTTCTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCG
 301 +-----+-----+-----+-----+-----+-----+-----+-----+ 348
 TAATGATGCAAGATGACCCCGGTTCGGTGGTGAGAGTGTGAGAGGAGC
 CDR3
 I T T F Y W G O G T T L T V S S -

FIG. 5A

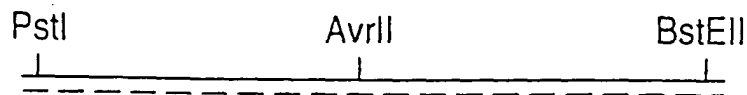
GACATTGAGCTGACCCAGTCTCCATCATCTCTGAGCGCATCTGTTGGAGATAGGGTCACT
1-----+-----+-----+-----+-----+-----+-----+ 60
CTGTAAGTCGACTGGGTCAGAGGTAGTAGAGACTCGCGTAGACAACTCTATATCCCACTGA
D I Q L T Q S P S S L S A S V G D R V T -
ATGAGCTGTAAGTCCAGTCAAAGTGTTTATACAGTGCAATCACAAAGAACTACTTGGCC
61-----+-----+-----+-----+-----+-----+-----+ 120
TACTCGACATTGAGGTCAGTTTCACAAAATATGTCACGTTTAGTGTTCTTGATGAACCGG
CDR1
M S C K S S Q S V L Y S A N H K N Y L A -
TGGTACCAGCAGAAACCAGGGAAGCACCTAAACTGCTGATCTACTGGGCATCCACTAGG
121-----+-----+-----+-----+-----+-----+-----+ 180
ACCATGGTCGTCCTTGGTCCCTTTCGTGGATTGACGACTAGATGACCCGCTAGGTGATCC
CDR2
W Y Q Q K P G K A P K L L I Y W A S T R -
GAATCTGGTGTCCTTCGCGATTCTCTGGCAGCGGATCTGGGACAGATTTTACTTTCACC
181-----+-----+-----+-----+-----+-----+-----+ 240
CTTAGACCACAGGGAAGCGCTAAGAGACCGTCGCGCTAGACCCCTGTCTAAAATGAAAGTGG
E S G V P S R F S G S G S G T D F T F T -
ATCAGCTCTCTTCAACCAGAAAGACATTGCAACATATTATTGTCACCAATACCTCTCCTCG
241-----+-----+-----+-----+-----+-----+-----+ 300
TAGTCGAGAGAAAGTTGGTCTTCTGTAAAGTTGTATATAATAACAGTGTTATGGAGAGGAGC
CDR3
I S S L Q P E D I A T Y Y C H Q Y L S S -
TGGACGTTCCGTTGGAGGGACCAAGCTGGAGATCAAACGT
301-----+-----+-----+-----+-----+-----+-----+ 339
ACCTGCAAGCCACCTCCCTGGTTCGACCTCTAGTTTGCA
W T F G G G T K L E I K R

FIG. 5B

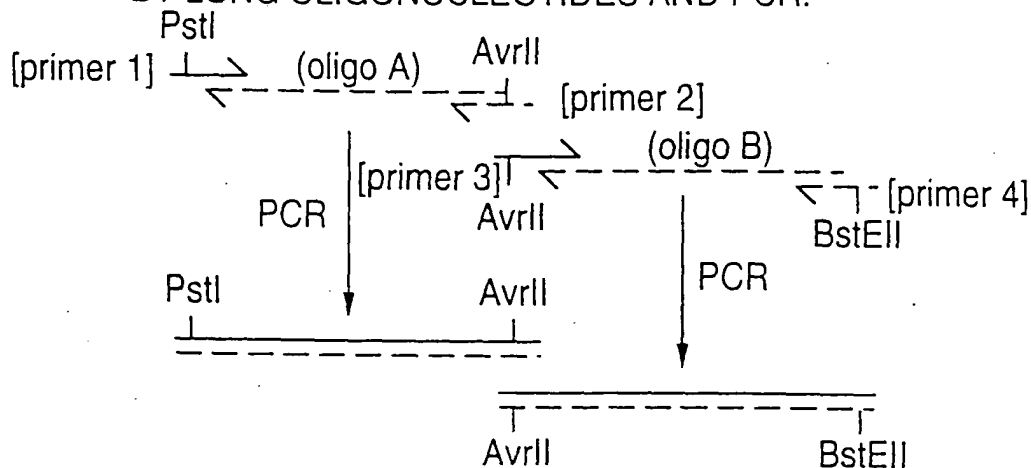
CAGTCCAGCTGGTCCAATCAGGGGCTGAAGTCAAGAAACCTGGGTCAATCAGTGAAGGTC
 1-----+-----+-----+-----+-----+ 60
 GTCCAGGTCCGACCAAGGTTAGTCCCCGACTTCAGTTCTTTGGACCCAGTAGTCACTTCCAG
 Q V Q L V Q S G A E V K K P G S S V K V -
 TCCTGCAAGGCTTCTGGCTACACCTTTACTAGTACTGGCTGCACCTGGGTCAGGCAGGCA
 61-----+-----+-----+-----+-----+ 120
 AGGACGTTCCGAAGACCGATGTGGAAATGATCGATGACCGACGTGACCCAGTCCGTCCTCGT
 CDR1
 S C K A S G Y T F T [S Y W L H] W V R Q A -
 CCTGCACAGGCTCTGGAATGGATGATACATTAATCCTAGGAATGATTACTAGTAC
 121-----+-----+-----+-----+-----+ 180
 GGACCTGTCCCAGACCTTACCTAACCTATGTAATTAGGATCCTTACTAATAATGACTCATG
 CDR2
 P G Q G L E W I G Y I N P R N D Y T E Y -
 AATCAGAACTTCAAGGACAAGGCCACAATAACTGCAGACGAATCCACCAATACAGCCTAC
 181-----+-----+-----+-----+-----+ 240
 TTAGTCTTGAAGTTCCCTGTTCCGGTGTTATTGACGCTCTGCTTAGGTGGTTATGTCGGATG
 [N Q N F K D] K A T I T A D E S T N T A Y -
 ATGGAGCTGAGCAGCCTGAGGTCTGAGGACACGGCATTTTATTTTGTGCAAGAGGGAT
 241-----+-----+-----+-----+-----+ 300
 TACCTCGACTCGTCGGACTCCAGACTCCTGTGCCGTAAATAAACAACACGTTCTTCCCTA
 M E L S S L R S E D T A F Y F C A R [R D] -
 ATTACTACGTTCTACTGGGGCCAAGCACCACGGTCACCGTCTCCTCG
 301-----+-----+-----+-----+-----+ 348
 TAATGATGCAAGATGACCCCGGTTCCGTGTCGCCAGTGCGCAGAGGAGC
 CDR3
 [I T T F Y] W G Q G T T V T V S S -

FIG. 6

DESIGNED SEQUENCE FOR HUMANIZED LL2 VH DOMAIN:



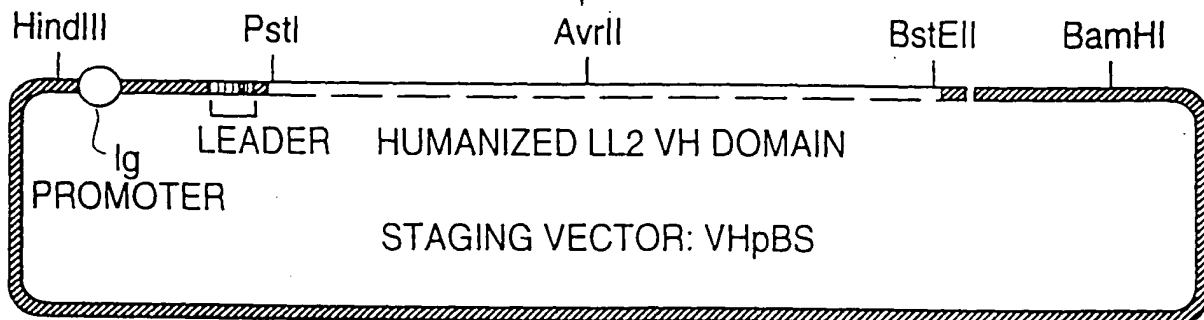
CONSTRUCTION OF THE HUMANIZED LL2 VH DOMAIN
BY LONG OLIGONUCLEOTIDES AND PCR:



PstI/AvrII DIGESTION

BstEII/AvrII DIGESTION

LIGATION TO THE PstI/BstEII
SITES OF THE HEAVY CHAIN
STAGING VECTOR: VHpBS



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FIG. 7

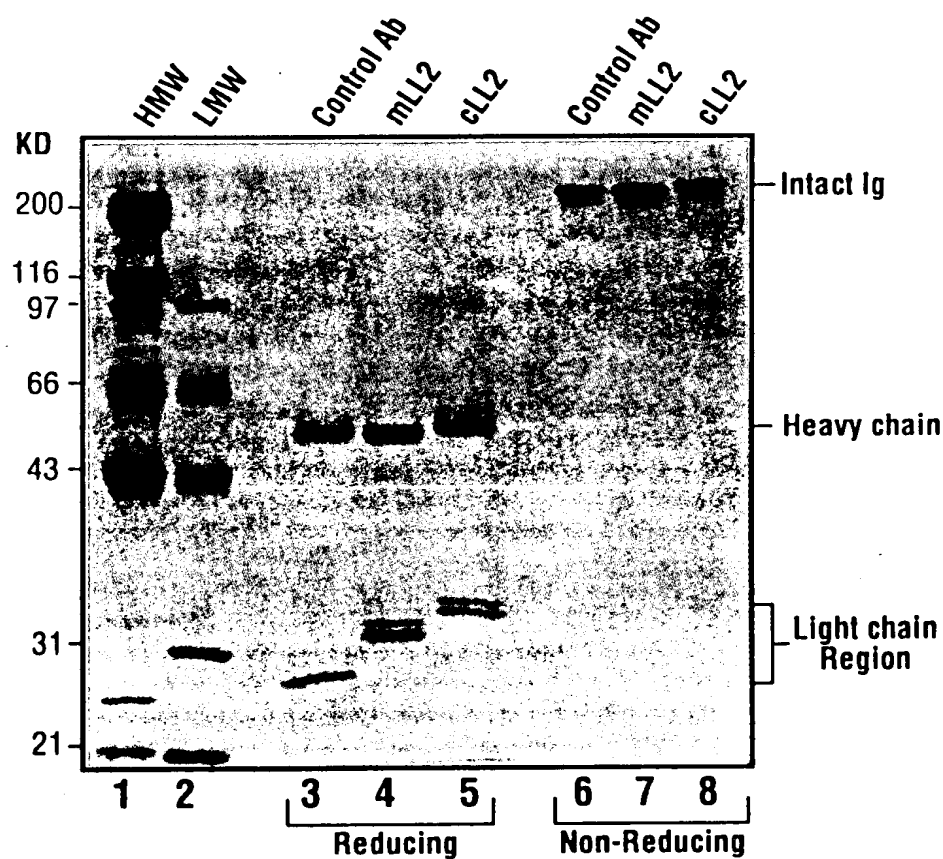


FIG. 8

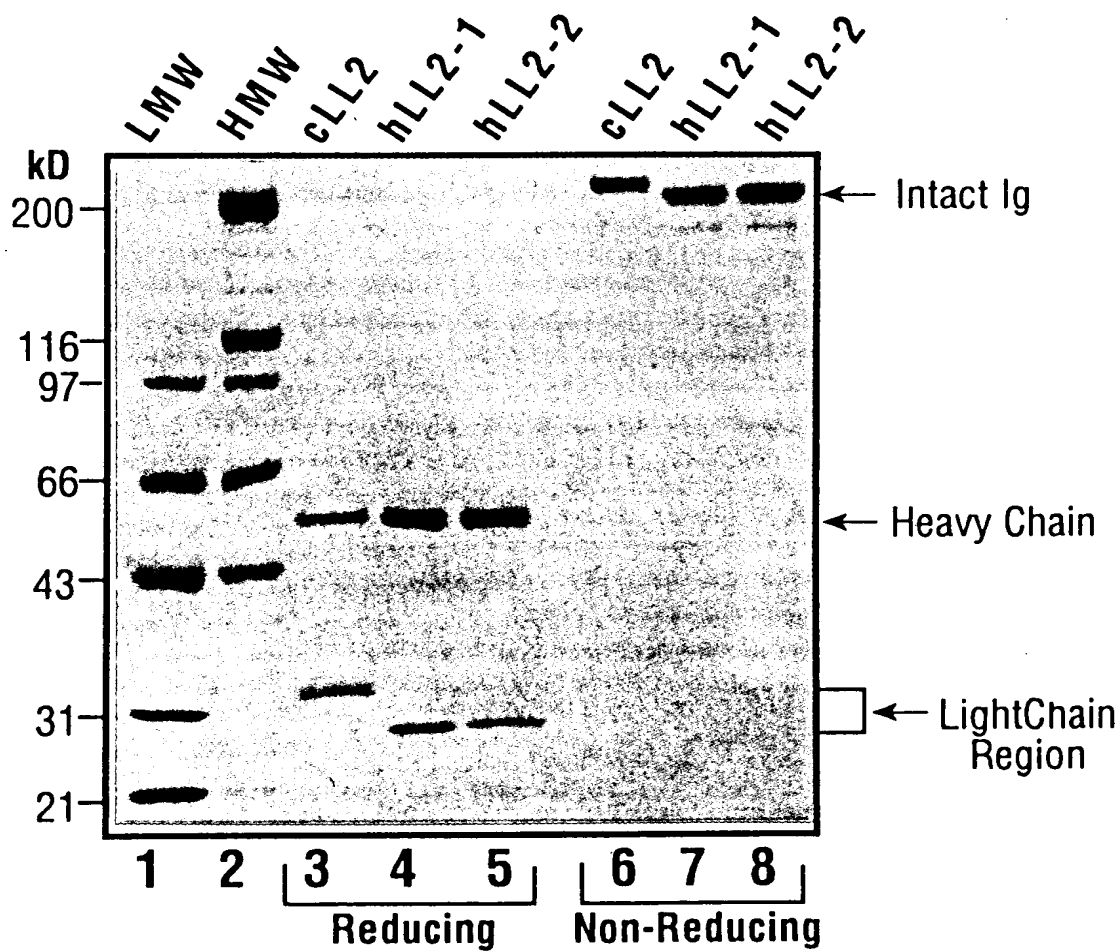


FIG. 9

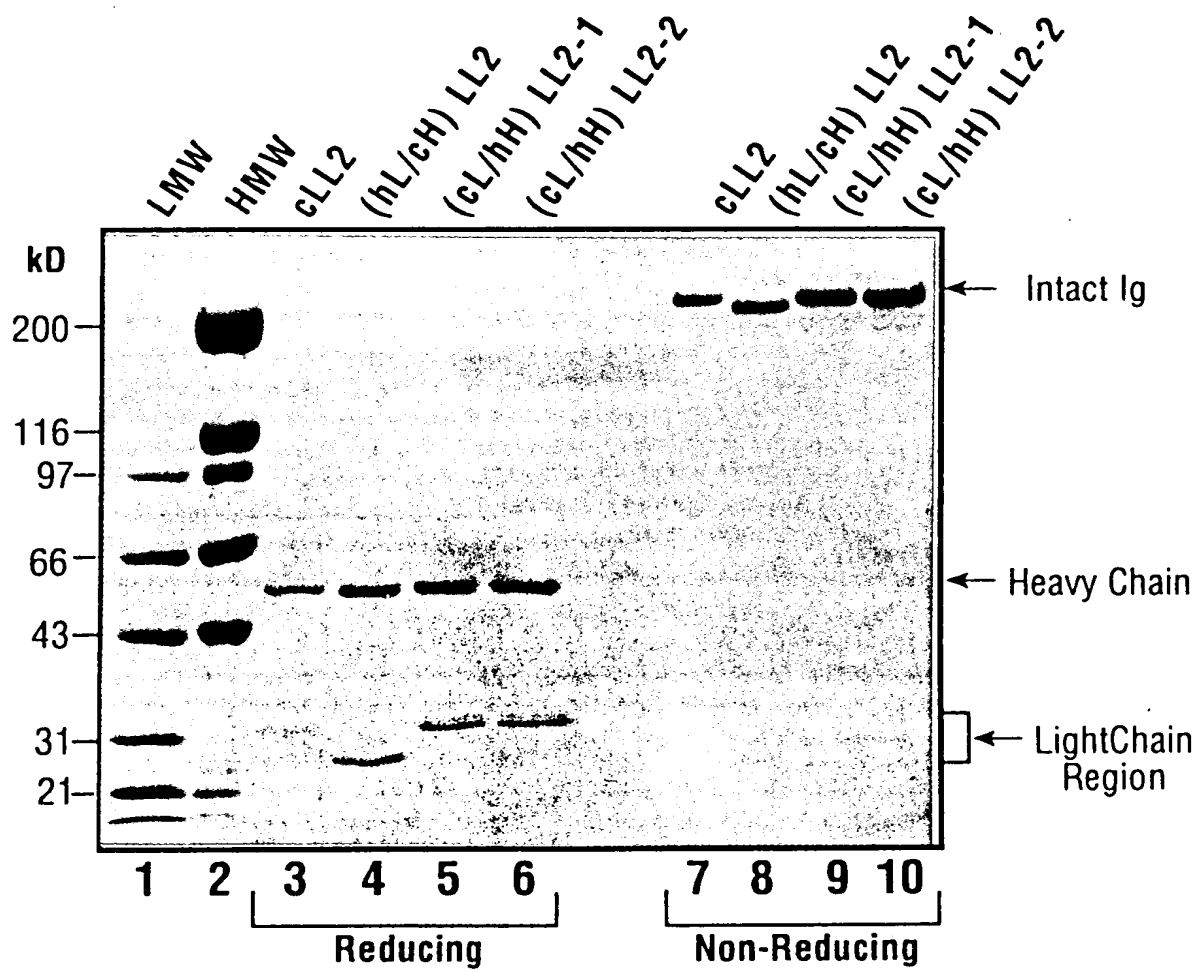


FIG. 10

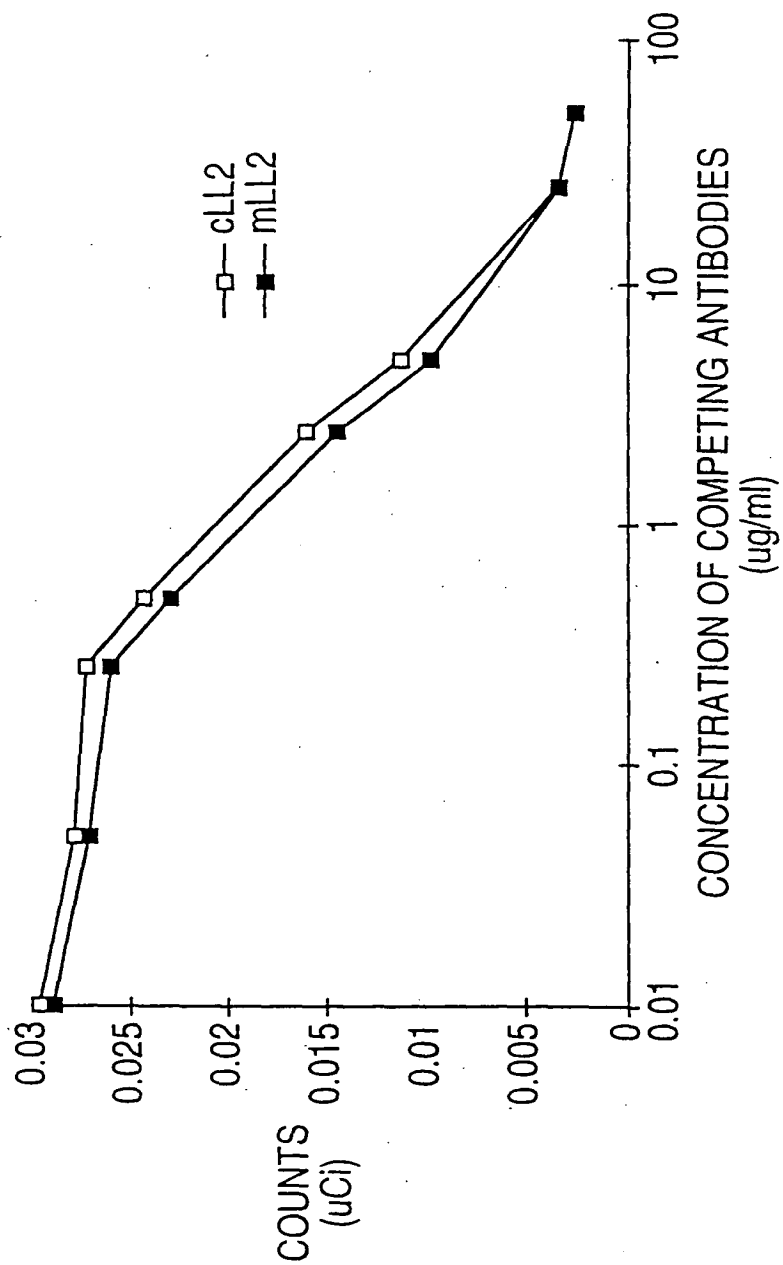


FIG. 11A

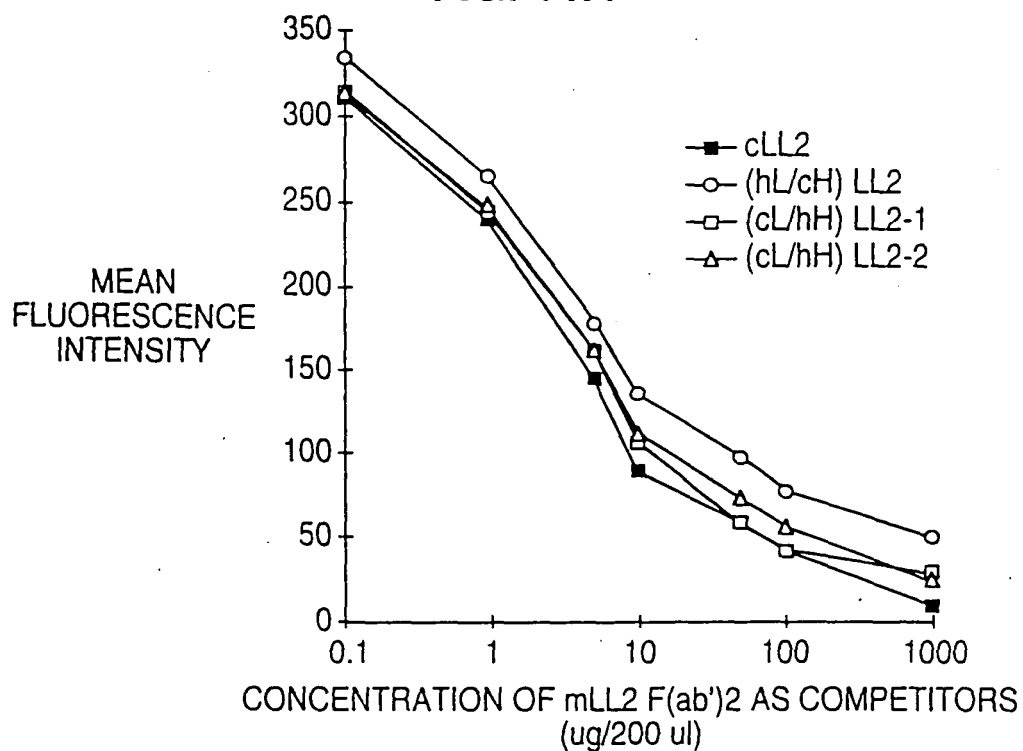


FIG. 11B

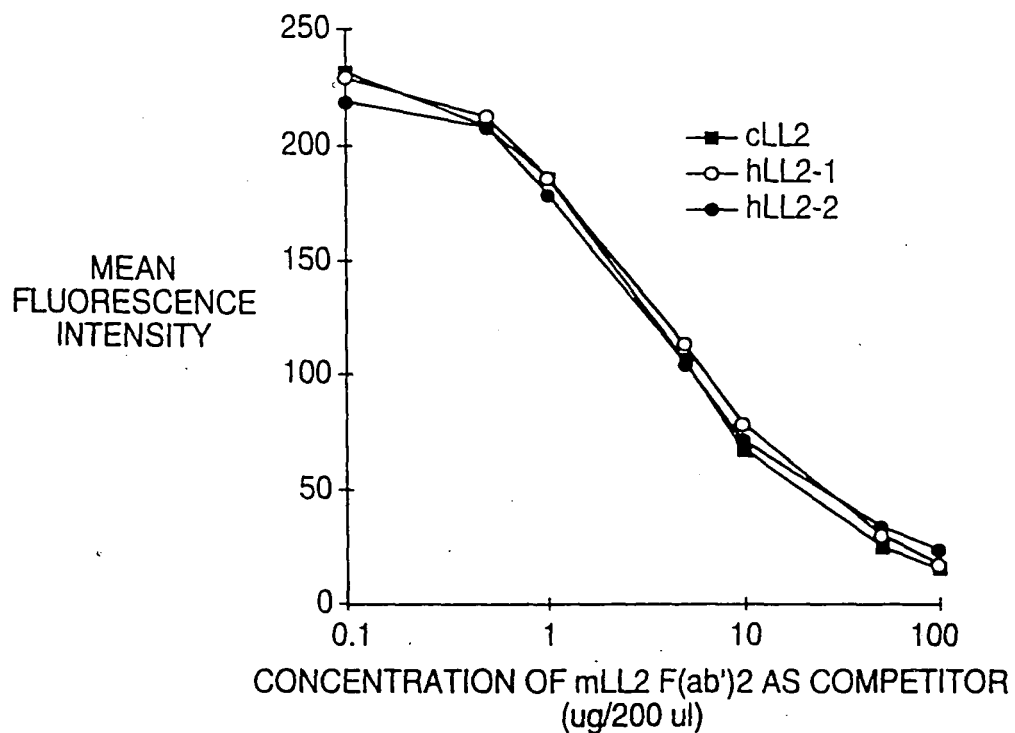


FIG. 12

INTERNALIZATION: c-LL2. h-LL2 vs. m-LL2 IN RAJI CELLS

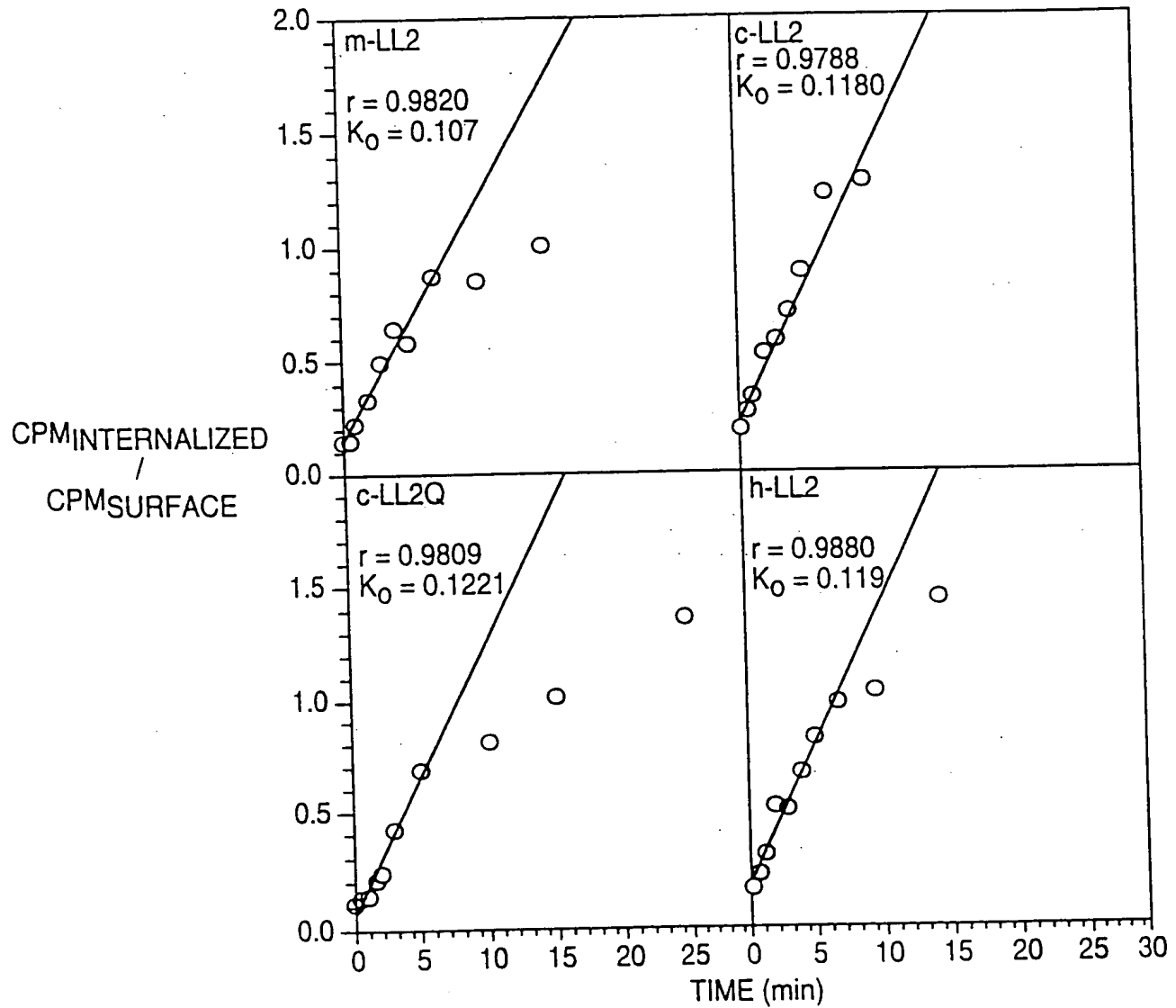
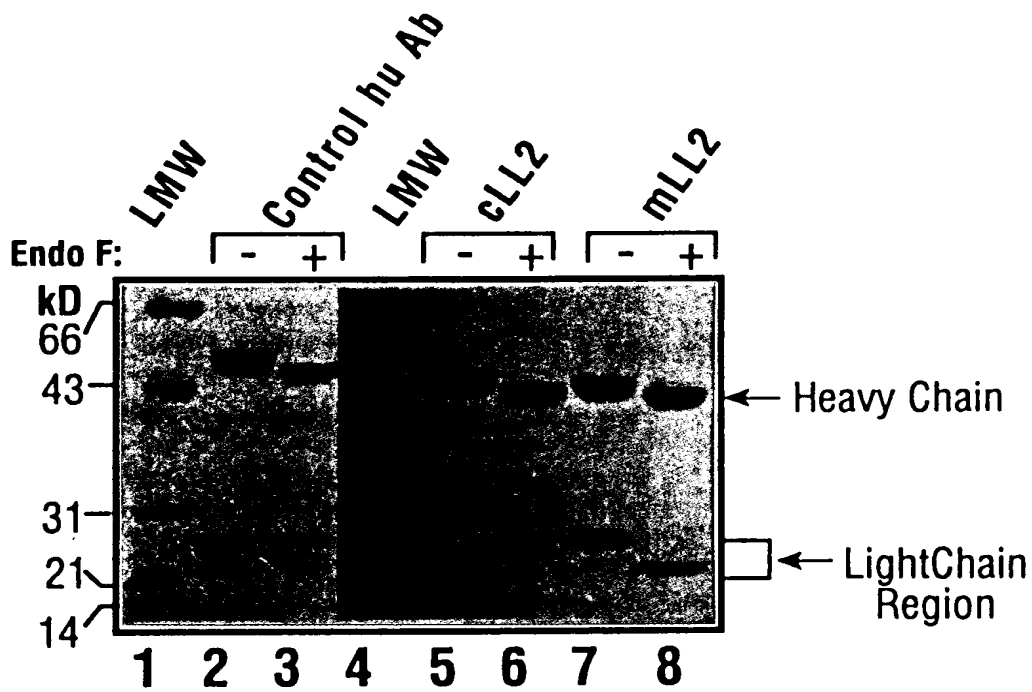


FIG. 13



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FIG. 14

